201-16365C

EPA/OPPT/High Production Volume (HPV) Challenge Program: Robust Summaries & Test Plans: 2-H-Benzimidazole-2-thione, 1,3-dihydro-4 (or 5)-methyl-, Zinc Salt (2:1); Response to EPA Comments June 12, 2003 and re-submission of Robust Summaries and Test Plans

Dear Mr. Hernandez:

RT Vanderbilt is providing responses to EPA comments and revised robust summaries and test plan for 2-H-Benzimidazole-2-thione, 1,3-dihydro-4 (or 5)-methyl-, Zinc Salt (2:1), which was posted on the ChemRTK HPV Challenge Program Web site on January 31, 2003.

Based on the submitted documentation, RT Vanderbilt considers its commitment to this chemical under EPA/OPPT/High Production Volume (HPV) Challenge Program to be complete.

Sincerely,

Erin Bendig
Product regulatory Specialist
RT Vanderbilt Company

Response to EPA Comments on Chemical RTK HPV Challenge Submission: Zinc Mercaptotoluimidazole

Summary of EPA Comments

The sponsor, the R. T. Vanderbilt Company, Inc., submitted a test plan and robust summaries to EPA for Zinc Mercaptotoluimidazole (CAS No. 61617-00-3) dated January 02, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 31, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. Adequate data are available for all endpoints except partition coefficient and water solubility for the purposes of the HPV Challenge Program. The submitter needs to measure the partition coefficient and to determine whether the methodology used to measure water solubility was appropriate. Agree.

2. Health Effects. EPA agrees with the proposal to conduct a combined repeated-dose, reproduction and developmental toxicity screening test. In addition, the submitter needs to conduct an in vitro mammalian chromosomal aberrations test and address deficiencies in the robust summaries. Agree

3. Ecological Effects. EPA agrees with the plan to conduct testing for the fish, invertebrate, and algal endpoints. In addition, a chronic toxicity study in daphnia is necessary if the measured log KOW is determined to be 4.2. A chronic Daphnia study is not necessary as the Log Kow is less than 4.2.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Zinc Mercaptotoluimidazole Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

Adequate data are available for all endpoints except partition coefficient and water solubility for the purposes of the HPV Challenge Program. Agree

Partition coefficient. The submitter states that an estimated value is adequate for this endpoint. EPA disagrees. The EPIWIN software was not designed to estimate values for organometallic compounds. The submitter needs to determine a measured value using OECD TG 107/117. Agree. The measured value using OECD 107 is 3.07. A summary has been added to the dossier.

Water solubility. The submitter reports a measured value of 32 mg/L conducted according to OECD TG 105 and GLP. It is unclear whether the study was conducted by the shake flask or the HPLC method. According to the guideline, the shake flask method should not be used if the water solubility is expected to be less than 0.01 g/L. In that region, the shake flask method may provide a higher value than the true solubility. Furthermore, the zinc derivative would be expected to be less soluble than the corresponding thiol, for which EPIWIN estimated a solubility of 3 mg/L. The submitter needs to clarify the methodology used and determine whether it was appropriate. The flask method was used for this material and as the solubility was found to be > 10mg/l the flask method is appropriate and valid. The method of detection i.e. HPLC or GC has no bearing on the method chosen for water solubility.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Adequate data are available for all environmental fate endpoints for the purposes of the HPV Challenge Program. Agree

Stability in water. The test plan states that this endpoint will be met using calculated data. However, HYDROWIN cannot estimate hydrolysis rate constants for metal salts. Therefore, the submitter should refer in the test plan to a "technical discussion" and add a discussion on the lack of hydrolyzable functional groups to the robust summary. Agree. VANOX® ZMTI antioxidant, is Zinc 2-mercaptotoluimidazole. The material is a very low water soluble zinc complex of 2-mercaptotoluimidazole. The material is not readily hydrolyzable, as it does not contain common hydrolysable organic functional groups such as carboxyl esters, nitriles and imines. Decomplexed, the free 2-mercaptotoluimidazole should also be resistant to hydrolysis, even though it is an imine-like material, due to the presence of a phenyl on the imine nitrogen.

Biodegradation. The submitter needs to correct the statement in the test plan summary that a ready biodegradation study is planned, which conflicts with the test plan. Agree. A biodegradation study was conducted previously. An additional test is not needed.

Fugacity. The submitter needs to provide input parameters in the robust summary. Agree. The additional information has been supplied in the dossier.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for the acute toxicity and gene mutation endpoints. EPA agrees with the submitter's proposal to conduct a combined repeated-dose, reproduction and developmental toxicity screening test following OECD TG 422. The submitter needs to address deficiencies in the robust summaries. Agree. This study is complete and robust summaries have been provided in the dossier.

Genetic toxicity (chromosomal aberrations). No data were submitted and no testing is proposed. EPA disagrees with the view that bacterial mutation studies serve as an "initial screen" for chromosomal aberration potential. The submitter needs to conduct an in vitro mammalian chromosomal aberrations test following OECD TG 473. Agree. This study is complete and a robust summary has been provided in the dossier.

Ecological Effects (fish, invertebrates, and algae)

EPA agrees with the submitter's plan to conduct testing for the fish, invertebrate, and algal endpoints. The tests should be conducted according to OECD TG's 201, 202, and 203, using mean measured concentrations. It would be helpful in interpreting the test results if concentration monitoring included the measurement of the equilibrium concentration of zinc ion and/or toluimidazolethiolate ion. Agree. These studies are complete and robust summaries have been provided in the dossier.

Chronic toxicity. If the measured log KOW from the recommended partition coefficient study is 4.2, chronic effects in aquatic organisms may occur. Therefore, additional testing to obtain chronic toxicity data on aquatic invertebrates is needed because this class of chemical may show both acute and chronic effects. The log Kow for this material has been determined to be less than 4.2 (=3.07) using OECD 107. A chronic effects on aquatic organisms is not needed.

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. The omitted information for the acute oral toxicity study included length of the observation period and a range or 95% confidence interval for the LD50. There is a discrepancy or a typographical error in the supporting data from the acute inhalation toxicity study: the LC50 (4 hr) was reported as > 2.03 mg/l, but the tested dose was 2.13 mg/l. Also, the OECD test guideline number for the acute inhalation toxicity study should be 403 instead of 073. Agree. The robust summaries have been revised.